Claims

We claim:

1. A method for screening for, detecting or diagnosing large granular lymphocyte (LGL) leukemia or an autoimmune disorder in a person or animal, said method comprising obtaining a biological sample from said person or animal, and screening for upregulated expression of a gene or genes, or a gene product thereof, whose expression is upregulated in LGL and/or screening for downregulated expression of a gene or genes, or a gene product thereof, whose expression is downregulated in LGL.

2. The method according to claim 1, wherein said gene or gene product whose expression is upregulated in LGL is selected from the group consisting of granzymes A, B, H, and K; cathepsin C and W; calpain small subunit; caspase-8; perforins; A 20; PAC-1; NGK2 receptors; RANTES; MIP-1alpha; MIP-1beta; IL-1 beta; IL-8; IL-1Ra; IFN-gamma; IL-18; IL-10; and IL-12 p35.

3. The method according to claim 1, wherein said gene or gene product whose expression is upregulated in LGL is selected from the group consisting of cystatin C and A; α-1 antitrypsin; and metalloproteinase inhibitor-8.

4. The method according to claim 1, wherein the expression of at least five, at least 10, at least 15, at least 20, at least 25, at least 30, at least 35, or at least 40 genes or gene products whose upregulation is present in LGL is determined.

5. The method according to claim 1, wherein the expression of at least five, at least 10, at least 15, at least 20, at least 25, at least 30, at least 35, or at least 40 genes or gene products whose downregulation is present in LGL is determined.

6. The method according to claim 1, wherein said biological sample is selected from the group consisting of bone marrow, lymph node, spleen, peripheral blood, lymph fluid, serous fluid, urine, and saliva.

7. A method for treating or preventing large granular lymphocyte (LGL) leukemia or an autoimmune disorder in a person or animal, said method comprising administering an effective amount of a composition that inhibits expression of a gene or genes, or that inhibits or blocks biological activity of a gene product, whose expression is upregulated in LGL and/or administering an effective amount of a composition that increases expression of a gene or genes, or that increases the amount of a gene product, whose expression is downregulated in LGL.

8. The method according to claim 7, wherein said gene or gene product whose expression is to be inhibited is selected from the group consisting of granzymes A, B, H, and K; cathepsin C and W; calpain small subunit; caspase-8; perforins; A 20; PAC-1; NGK2 receptors; RANTES; MIP-1alpha; MIP-1beta; IL-1 beta; IL-8; IL-1Ra; IFN-gamma; IL-18; IL-10; and IL-12 p35.

9. The method according to claim 7, wherein said gene or gene product whose expression is to be increased is selected from the group consisting of cystatin C and A; α-1 antitrypsin; and metalloproteinase inhibitor-8.

10. A composition for treating or preventing large granular lymphocyte (LGL) leukemia or an autoimmune disorder in a person or animal, said composition comprising a means for inhibiting expression of a gene, or inhibiting or blocking biological activity of a protein encoded by a gene, whose expression is upregulated in LGL.

11. The composition according to claim 10, wherein said composition comprises an antisense polynucleotide whose transcribed sequence is at least partially complementary to the transcribed sequence of a gene whose expression is upregulated in LGL, wherein expression of said gene is inhibited or blocked by expression of said antisense polynucleotide.

12. The composition according to claim 11, wherein said gene is selected from the group consisting of granzymes A, B, H, and K; cathepsin C and W; calpain small subunit; caspase-8; perforins; A 20; PAC-1; NGK2 receptors; RANTES; MIP-1alpha; MIP-1beta; IL-1 beta; IL-8; IL-1Ra; IFN-gamma; IL-18; IL-10; and IL-12 p35.

13. The composition according to claim 10, wherein said composition comprises an RNA interfering molecule.

14. The composition according to claim 13, wherein said RNA interfering molecule inhibits expression of a gene selected from the group consisting of granzymes A, B, H, and K; cathepsin C and W; calpain small subunit; caspase-8; perforins; A 20; PAC-1; NGK2 receptors; RANTES; MIP-1alpha; MIP-1beta; IL-1 beta; IL-8; IL-1Ra; IFN-gamma; IL-18; IL-10; and IL-12 p35.

15. The composition according to claim 13, wherein said RNA interfering molecule is a short interfering double-stranded RNA.

16. The composition according to claim 10, wherein said composition comprises:

a)   an antibody, or an antigen binding fragment thereof, that specifically binds to said protein and blocks biological activity of said protein;

b)   an antibody, or an antigen binding fragment thereof, that specifically binds to a receptor for said protein and prevents or inhibits binding of said protein to said receptor;

c)   a peptide that binds to said protein or said receptor and block biological activity of said protein or said receptor; or

d)   a combination of any of said antibody or peptide.

17. A composition for treating or preventing large granular lymphocyte (LGL) leukemia or an autoimmune disorder in a person or animal, said composition comprising a means for

increasing expression or levels of a protein encoded by a gene whose expression is downregulated in LGL.

18. A method for screening for a compound useful in treating or preventing LGL or an autoimmune disorder in a person or animal, wherein said method comprises contacting an LGL cell with a test compound, isolating nucleic acid from said cell, and screening for: 1) inhibition of those gene sequences that are upregulated in LGL, or 2) increased expression of those gene sequences that are downregulated in LGL, or 3) both screening for inhibition of those gene sequences that are upregulated in LGL and screening for increased expression of those gene sequences that are downregulated in LGL are performed.